

ALLERGEN PACK DERMATOPHAGOIDES FARINAE-
Alvix Laboratories, LLC

ALLERGEN PACK DERMATOPHAGOIDES FARINAE

BOXED WARNING

WARNING: ANAPHYLAXIS

Do not inject intravenously.

Allergenic extracts may potentially elicit a severe lifethreatening systemic reaction, rarely resulting in death.

This allergenic product is intended for use only by physicians who are experienced in the administration of allergenic extracts and the emergency care of anaphylaxis, or for use under the guidance of an allergy specialist.

The initial dose must be based on skin test.

Observe patients in the office for at least 30 minutes following treatment. Emergency measures and personnel trained in their use must be available immediately in the event of life threatening reaction.

Immunotherapy may not be suitable for patients with medical conditions that reduce their ability to survive a systemic reaction, including significant cardiovascular and/or pulmonary diseases. Patients who are receiving beta blockers may be unresponsive to the usual doses of epinephrine used to treat systemic reactions, including anaphylaxis.

DESCRIPTION

Greer Standardized Mite (*Dermatophagoides farinae* and/or *Dermatophagoides pteronyssinus*) extracts are sterile solutions used for intradermal testing or subcutaneous immunotherapy. Each vial contains 5,000, 10,000, or 30,000 Allergy units/mL of sterile mite extract (*D. farinae* and/or *D. pteronyssinus*), 50% glycerin v/v, and 0.4% phenol (preservative). Inert ingredients include 0.50% sodium chloride for isotonicity and 0.25% sodium bicarbonate as a buffer. For immunotherapy, concentrated extracts are diluted in normal saline, buffered saline, albumin saline or 10% glycerosaline based on patient's reactivity. For intradermal testing, extracts may be diluted in normal saline, buffered saline, or albumin saline.

Source materials for the extract are whole mite bodies. The mites are cultured, handled, and cleaned to remove at least 99% of the food medium. The medium contains no material of human origin.

The mite extract is standardized by comparison to a reference preparation supplied by the Center for Biologics Evaluation and Research of the FDA, labeled 10,000 Allergy Unit/mL. The relative potency of the extract is determined by ELISA inhibition compared to the FDA mite reference, and is labeled in Allergy Unit/mL.

CLINICAL PHARMACOLOGY

Dust mites belonging to the genus *Dermatophagoides* are indoor allergens found in humid geographic locations worldwide. *D. farinae* and *D. pteronyssinus* occur widely with most homes in the United States coinhabited by both species.

Mechanism of Action

The complete mechanisms of allergen immunotherapy are not clear and remain the subject of investigation. The allergic reaction is dependent on the presence of allergen-specific immunoglobulin E (IgE) antibodies that are bound to specific receptors on mast cells and basophils. The presence of IgE antibodies sensitizes these cells, and upon interaction with the appropriate allergens, histamine and other mediators are released which produce local or systemic responses in sensitive individuals, and characteristic symptoms of atopic diseases, such as allergic rhinitis and allergic asthma. Changes in serum antibody and T-lymphocyte responses resulting from immunotherapy have been demonstrated, and these changes often correlate closely with clinical (symptom) improvements. Specific mechanisms may vary depending on the nature of the allergic disease, the allergenic specificities of patients and populations, extract formulations, route of administration, dose and duration of treatment.²

Subcutaneous administration of allergenic extracts is known to elicit numerous immunological changes that are both time and dose-dependent. Many of these changes appear to be related to (or a precursor to) improvements in symptoms and other clinical parameters, as noted above. Specific changes found after immunotherapy with dust mite extracts include significant increases in mite-specific IgG4 antibodies¹², interleukin-10-positive T cells, and several T-cell receptors, and significant decreases in serum nitric oxide, eosinophil cationic protein, interleukin-4-positive T cells and IgE-mediated basophil histamine release.¹³

NONCLINICAL TOXICOLOGY

Carcinogenesis & Mutagenesis & Impairment of Fertility Section

No studies in animals have been performed to evaluate carcinogenicity, mutagenicity or impairment of fertility.

CLINICAL STUDIES

The dust mites *D. farinae* and *D. pteronyssinus* are the major source of allergens in house dust¹⁴. The efficacy of immunotherapy for Type I hypersensitivity (i.e., allergy) to airborne allergens^{2,15,16} including dust mite has been well established. Specifically, immunotherapy for allergic hypersensitivity to house dust mite allergens has been addressed in a 1995 Cochrane meta-analysis of 20 randomized, controlled trials of immunotherapy¹⁷, and two subsequent updated Cochrane meta-analysis published in 1999¹⁸ and 2003¹⁹. In addition, efficacy for immunotherapy in rush or cluster protocols, in which the dose escalation is compressed over days or weeks, has also been demonstrated^{20, 21}.

INDICATIONS AND USAGE

Greer Standardized Mite (*Dermatophagoides farinae* and/or *Dermatophagoides pteronyssinus*) Extracts are allergenic extracts indicated for:

- skin test diagnosis of mite allergy
- treatment of patients with mite-induced allergic asthma, rhinitis and conjunctivitis.

For Immunotherapy, patients must show hypersensitivity to *Dermatophagoides farinae* (*D. farinae*) or *Dermatophagoides pteronyssinus* (*D. pteronyssinus*) based on their clinical history, allergen exposure history, and skin test reactivity.

DOSAGE AND ADMINISTRATION

Do not inject intravenously.

Greer Standardized Mite extracts are diluted with sterile diluent for allergenic extracts when used for intradermal testing or subcutaneous immunotherapy. Dosages vary by mode of administration, and by individual response and tolerance. Parenteral drug products should be inspected visually for particulate

matter and discoloration prior to administration, whenever solution and container permit.

Greer Standardized Mite Extracts should be a light brown solution that is free of particulate matter. If particulate matter is observed then the solution should be discarded.

Diagnostic Testing

For diagnosis of a patient with a suspected allergy to either species of dust mite (*D. farinae* or *D. pteronyssinus*), diagnostic skin testing should include the standardized mite mixture or the single-species mite extracts.

- If a skin test with the standardized mite mixture elicits a positive reaction, then the single-species mite extracts can be used to determine the degree of sensitivity to each, and to guide in the selection of extracts and their concentration for immunotherapy, if indicated.
- A positive skin test reaction to any allergen must be interpreted in light of the patient's history of symptoms, the time of year, and known exposure to environmental allergens.

Percutaneous Skin Testing

For percutaneous (scratch, prick, or puncture) testing, use 10,000 Allergy Units/mL Greer Standardized Mite Extract stock concentrate in dropper vials. If patient is suspected of having exquisite sensitivity, such as anaphylaxis, to certain foods and drugs, initiate percutaneous testing with several serial 10-fold dilutions of the usual test concentration.

- For scratch tests, scarify the skin, and then apply one drop of the extract to the scratch.
- For prick tests, place one drop of extract on the skin and pierce through the drop into the skin with a slight lifting motion.
- For puncture tests, place one drop of extract on the skin and pierce through the drop perpendicular to the skin.

When using percutaneous test devices, follow the directions provided with the test devices.

Include a positive control to detect false negative responses to skin testing, which may occur if serum levels of antihistamines remain from prior medication administration [see Drug Interactions (7.2)]. A glycerinated histamine phosphate diluted to 10mg/mL (6mg/mL histamine base) may be used as the positive control.

Include a negative control to detect false positive responses, which can occur when the patient has a non-specific reaction to the diluent. A 50% glycerosaline solution may be used as the negative control. Read skin tests 15-20 minutes after exposure. Record the induration (wheal) and erythema (flare) response by noting the longest diameter of each, or by the sum of the longest erythema diameter and the mid-point orthogonal diameters of erythema (OE).

Percutaneous testing devices often have their own grading systems, as these devices may cause different degrees of trauma to the skin and deliver different volumes of allergenic extract. Follow grading instructions for the device used.

Intradermal Skin Testing

Intradermal tests are commonly used when the reaction to percutaneous testing is negative or equivocal but the patient has a strong clinical history of symptoms triggered by exposure to a specific allergen. Because immediate systemic reactions are more common with intradermal testing, prescreening with percutaneous testing is a practical safety measure.¹

Dilute the stock concentrate with sterile diluent. Use saline with human serum albumin (HSA), buffered saline, or saline. If prescreening is not done, or if patients are expected to be high risk, precautions should be observed since some patients have experienced anaphylaxis and death.

- Patients who do not react to percutaneous skin testing should be tested intradermally at a starting dose of 0.02 to 0.05 mL of a 50 Allergy Units/mL extract dilution.
- Patients suspected of being highly allergic should first receive a test dose of 0.02 to 0.05 mL of a 0.05 Allergy Units/mL extract dilution.
- If the initial dose test is negative, subsequent intradermal tests using increasingly stronger doses may be performed up to the maximum recommended strength of 200 Allergy Units / mL.
- If percutaneous skin testing was not performed, include a positive control to detect false negative responses to skin testing, which may occur if serum levels of antihistamines remain from prior medication administration [see Drug Interactions (7.2)]. A glycerinated histamine phosphate diluted to 0.5 mg/mL (0.18 mg/mL histamine base) or aqueous histamine phosphate 0.275 mg/mL (0.1 mg/mL histamine base) may be used as the positive control.
- If percutaneous skin testing was not performed, include a negative control to detect false positive responses, which can occur when the patient has a non-specific reaction to the diluent. A 1% glycerin in 0.9% saline solution may be used as the negative control.
- Measure the wheal-and-flare response after 15-20 minutes, which may be graded using various methods as described in the instructions for the device used.

The mean dose of Greer dust mite allergen required to elicit a positive intradermal test result (ØE ³ 50 mm) in a total of 83 mite puncture test

positive (ØE ³ 20 mm) persons is shown in Table 1.

Table 1. Intradermal Reactivity to Mite Allergens

Allergen	Number of Persons	Dose to Elicit 50 mm Sum of Diameter Erythema Reaction	
		Mean (AU*/mL)	Range (AU/mL)
D. farinae	46	0.00856	0.00004 - 1.75935
D. pteronyssinus	37	0.00570	0.00002 - 1.36341**

* Allergy Units

** Data is available on file with Greer

Immunotherapy

Subcutaneous injection only.

Subcutaneous injections for immunotherapy should be prepared by dilution of stock concentrate based on patient's reactivity. Stock concentrations of Greer Standardized Mite Extract are available in 5,000 Allergy Units/mL, 10,000 Allergy Units/mL, 30,000 Allergy Units/mL for immunotherapy. See Table 2 for dilution preparation. Also see Dosage Modification Guidelines. (2.2.1)

- The initial dose of the extract should be based on the percutaneous test reactivity. In patients who appear to be exquisitely sensitive by history and skin test, the initial dose of the extract should be 0.1 mL of a 0.005 to 0.05 Allergy Units/mL dilution. Patients with lesser sensitivity may be started

at a 0.5 to 5 Allergy Units/mL dilution.

- The dose of allergenic extract is increased at each injection by no more than 50% of the previous dose, and the next increment is governed by the response to the last injection.
- Large local reactions which persist for longer than 24 hours are generally considered an indication for repeating the previous dose or reducing the dose at the next administration.
- Any evidence of a systemic reaction is an indication for a significant reduction (at least 75%) in the subsequent dose. Repeated systemic reactions, even of a mild nature, are sufficient reason for the cessation of further attempts to increase the reaction-causing dose.
- Severe reactions require a decrease in the next dose by at least 50%. Proceed cautiously in subsequent dosing.
- A maximum tolerated maintenance dose should be selected based on the patient's clinical response and tolerance. Doses larger than 0.2 mL of the concentrate are rarely administered because an extract in 50% glycerin may cause discomfort upon injection.
- Since the two mite species tend to cross-react, consider the total Allergy Units content in determining the maximum maintenance dose of the mixture.

Dosage Modifications Guidelines for Immunotherapy

The following conditions may indicate a need to withhold or reduce the dosage of immunotherapy. In situations prompting dose reduction, once the reduced dose is tolerated, a cautious increase in dosage can be attempted. Immunotherapy should be withheld or reduced in dosage if the following concurrent conditions exist:

- Severe symptoms of rhinitis and/or asthma;
- Infection accompanied by fever; or
- Exposure to excessive amounts of clinically relevant allergen prior to a scheduled injection.

Changing to a different lot of extract: All extracts lose potency over time. A fresh extract may have an effective potency that is substantially greater than that of older extracts. Therefore, the first dose from the fresh vial should not exceed a 25% increase of the previous dose or a 75% reduction of the previous dose, assuming both extracts contain comparable amounts of allergen, defined by Allergy Units.

Unscheduled Gaps between Treatments: Patients may lose tolerance for allergen injections during prolonged periods between doses, thus increasing their risk for an adverse reaction. The duration of tolerance between injections varies from patient to patient.

- During the build-up phase, when patients receive injections 1 to 2 times per week, it is customary to repeat or even reduce the extract dosage if there has been a substantial time interval between injections. This depends on 1) the concentration of allergen immunotherapy extract that is to be administered, 2) a previous history of systemic reactions, and 3) the degree of variation from the prescribed interval of time, with longer intervals since the last injection leading to greater reductions in the dose to be administered. This suggested approach to dose modification due to unscheduled gaps between treatments during the build-up phase is not based on published evidence. The individual physician should use this or a similar protocol as a standard operating procedure for the specific clinical setting.
- Similarly, if large unscheduled gaps occur during maintenance therapy, it may be necessary to reduce the dosage. The individual physician should devise a protocol as a standard operating procedure for his or her specific clinical setting in determining how to modify doses of allergen immunotherapy due to unscheduled gaps in treatment.

The extract previously used is from another manufacturer: Since manufacturing processes and sources of raw materials differ among manufacturers, the interchangeability of extracts from different manufacturers cannot be assured. The starting dose of the extract from a different manufacturer should be greatly decreased even though the extract is the same formula and dilution. In general, a dose reduction of 50- 75% of the previous dose should be adequate, but each situation must be evaluated separately considering the patient's history of sensitivity, tolerance of previous injections, and other factors. Dose intervals should not exceed one week when rebuilding dose.

The previous extract has expired or is near expiry: The dating period for allergenic extracts indicates the time that they can be expected to remain potent under ideal storage conditions (2° - 8°C) [see How Supplied/Storage and Handling (16)]. Some loss of potency occurs even when stored under ideal conditions, therefore extracts should not be stored beyond the expiration date. Instead, a new lot should be used (see "Changing to a different lot of extract", above)

Changing from non-stabilized to human serum albumin (HSA) stabilized diluents: Allergenic extracts diluted with HSA and 0.4% phenol are more potent than extracts diluted with diluents that do not contain stabilizers. When switching from a non-stabilized to an HSA stabilized diluent, consider lowering the dose for immunotherapy.

Administration of Immunotherapy

- Administer immunotherapy by subcutaneous injection in the lateral aspect of the arm or thigh. Avoid injection directly into any blood vessel.
-
- The optimal interval between doses of allergenic extract varies among individuals. Injections are usually given 1 or 2 times per week until the maintenance dose is reached, at which time the injection interval is increased to 2,3, and finally 4 weeks.
- Because most adverse reactions occur within 30 minutes after injection, patients should be kept under observation for at least 30 minutes.² For high risk patients 30 minutes of observation may not be sufficient.

Dilution Preparation

To prepare dilutions for intradermal testing and immunotherapy, start with a 5,000, 10,000, or 30,000 Allergy Units/mL stock concentrate, and prepare a 1:10 dilution by adding 0.5 mL of concentrate to 4.5 mL of sterile aqueous diluent. Subsequent dilutions are made in a similar manner (see Table 2).

Table 2. Ten-fold Dilution Series for intradermal testing and immunotherapy

Dilution	Extract	Diluent	AU*/mL	AU/mL	AU/mL
0	Concentrate		5,000	10,000	30,000
1	0.5 mL Concentrate	4.5 mL	500	1,000	3,000
2	0.5 mL Dilution 1	4.5 mL	50	100	300
3	0.5 mL Dilution 2	4.5 mL	5	10	30
4	0.5 mL Dilution 3	4.5 mL	0.5	1	3
5	0.5 mL Dilution 4	4.5 mL	0.05	0.1	0.3
6	0.5 mL Dilution 5	4.5 mL	0.005	0.01	0.03

*Allergy Units

DOSAGE FORMS AND STRENGTHS

For immunotherapy, concentrated extracts are diluted in normal saline, buffered saline, albumin saline or 10% glycerosaline. For intradermal testing extracts may be diluted in normal saline, buffered saline, or albumin saline.

Greer Standardized Mite Extract *D. farinae* and Greer Standardized Mite Extract *D. pteronyssinus* are supplied as stock concentrates containing 10,000 Allergy Unit/mL and Greer Standardized Mite Extract mixture (*D. farinae* and *D. pteronyssinus*) is supplied as a stock mixture concentrate containing 5,000 Allergy Units/mL of each species for use in percutaneous skin testing.

Greer Standardized Mite Extract *D. farinae* and Greer Standardized Mite Extract *D. pteronyssinus* are supplied as stock concentrates containing 5,000, 10,000, or 30,000 Allergy Unit/mL. Greer Standardized Mite Extract mixture (*D. farinae* and *D. pteronyssinus*) is supplied as a stock mixture concentrate containing 5,000 and 15,000 Allergy Units/mL of each species for use in intradermal testing and immunotherapy.

WARNINGS AND PRECAUTIONS

Serious Systemic Reactions

All concentrates of Greer Standardized Mite Extracts have the ability during skin testing and immunotherapy to elicit serious systemic reactions including anaphylactic shock and death [see Adverse Reactions (6)]. A review of the literature indicates that the incidence of near-fatal reactions to immunotherapy, defined as severe respiratory compromise, hypotension, or both, and requiring emergency treatment with epinephrine, has been estimated at 5.4 events per million injections in a 10-year retrospective survey of allergists.³ Fatalities from immunotherapy injections have been estimated to occur at a rate of approximately one death per 2.0 to 2.8 million injections in 4-, 10- and 12-year retrospective surveys of allergists.⁴⁻⁶ Because of the danger of serious reactions, caution is required in testing and treating high risk patients and those with medical conditions that reduce their ability to survive a serious systemic adverse event.

High-risk patients are defined as those patients:

- with labile or steroid-dependent asthma, particularly in those suffering an exacerbation of their symptoms at the time of extract administration;
- with extreme sensitivity to a particular allergen(s);
- who are currently using beta blockers;
- who are receiving an accelerated immunotherapy build-up schedule (e.g., rush immunotherapy);
- who are being changed from one allergenic extract to another;
- who are receiving high doses of allergenic extracts.

High risk patients have had fatal reactions. In addition, patients not high risk but on beta blockers have had fatal reactions because beta blockers interfere with beta adrenergics such as epinephrine used in treatment of anaphylaxis.

Patients should be kept under observation for a minimum of 30 minutes after receiving allergenic extracts so that any adverse reaction can be observed and properly handled.²

Medications to treat systemic reactions, as well as emergency equipment should be available for immediate use. Extracts must only be administered by persons who are aware of the risk of systemic reactions, including anaphylaxis; are capable of handling such reactions; and have the necessary drugs and equipment on hand to do so.

Patients on Beta Blockers

Patients receiving beta blockers may be unresponsive to the usual doses of epinephrine used to treat

serious systemic reactions, including anaphylaxis. Inhalant allergy immunotherapy should be approached with caution in patients taking beta blockers. The risks of anaphylaxis in these patients should be carefully weighed against the benefits of immunotherapy [see Drug Interactions (7.1)].

Autoimmune Disease

Immunotherapy should be given cautiously to patients with other immunologic diseases and only if the risk from exposure to the allergen is greater than the risk of exacerbating the underlying disorder².

ADVERSE REACTIONS

Systemic reactions consist primarily of allergic symptoms, such as generalized skin erythema, urticaria, pruritus, angioedema, rhinitis, wheezing, laryngeal edema, and hypotension. Additional symptoms that are not usually associated with allergy also may occur, such as nausea, emesis, abdominal cramps, and diarrhea. Serious reactions may cause shock, loss of consciousness, and even death. Based on published studies,^{7,8} systemic reactions occur in less than 1% of patients receiving conventional immunotherapy to greater than 36% in some studies of patients receiving rush immunotherapy.

Local reactions at the injection site are the most commonly occurring reactions (e.g., erythema, itching, swelling, tenderness, pain). Although most adverse systemic reactions occur within 30 minutes of injection (some within minutes of extract exposure), such reactions also can occur up to six hours after skin tests of immunotherapy [see Dosage and Administration (2.2)]⁹.

DRUG INTERACTIONS

Beta Adrenergic Drugs

Patients receiving beta blocker drugs may not be responsive to beta adrenergic drugs used to treat anaphylaxis¹⁰, and may wish to temporarily postpone treatment day of skin testing. All such decisions should be made in consultation with the physician. [see Warnings and Precautions (5.2)].

Antihistamines

Skin testing with allergenic extracts should not be performed within 2-3 days of first-generation H₁-histamine receptor blockers (e.g., clemastine, diphenhydramine) and within 3 to 10 days of second-generation antihistamines (e.g., loratadine, terfenadine), except for astemizole, which requires an interval of 30-60 days between allergenic extract exposure and use. These products suppress histamine skin test reactions and could mask a positive response.

Topical Corticosteroids and Topical Anesthetics

Topical corticosteroids may suppress skin reactivity and should be discontinued at the skin test site for at least 2-3 weeks before skin testing. Topical local anesthetics may suppress flare responses and should be avoided at skin test sites.

Tricyclic Antidepressants

Tricyclic antidepressants can have potent antihistamine effects and will affect skin testing. Since use of tricyclics may alter skin test results, dosing for both skin testing and immunotherapy should be done with caution. If tricyclic medication has been recently discontinued, allow 7-14 days prior to skin testing to obviate the antihistamine effect. The risk of anaphylaxis in these patients should be carefully weighed against the risks and benefits of stopping tricyclics.

Other Drugs

The suppressive action of other drugs should be considered and emphasizes the need for a histamine positive control test.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category C:

Animal reproduction studies have not been conducted with Greer Standardized Mite Extracts. It is also not known whether Greer Standardized Mite Extracts can cause fetal harm when administered to a pregnant woman or whether they can affect reproduction capacity. Standardized Mite Extracts should be given to a pregnant woman only if clearly needed. Studies have not been performed in animals to determine whether extracts affect fertility in males or females, have teratogenic potential, or have other adverse effects on the fetus. Exercise caution in testing or treating pregnant females because a systemic reaction may cause maternal cardiovascular compromise leading to fetal distress with sequelae.

Nursing Mothers

It is not known whether allergenic extracts or their antigens are excreted in human milk. Because many drugs are excreted in human milk, exercise caution when extracts are administered to a nursing woman.

Pediatric Use

No studies have systematically examined differences in response to immunotherapy among child and adult patients. Children appear to tolerate injections of allergenic extracts very well.² Very young children (under age 5) can have difficulty cooperating with an immunotherapy program and for this reason, the physician should consider the benefits and risks of immunotherapy and individualize treatment in patients under the age of 5 years. [See Warnings and Precautions (5)].

Geriatric Use

Clinical studies of Greer Standardized Mite Extract did not include sufficient numbers of subjects aged 65 and older to determine whether they respond differently from younger subjects. Other reported clinical experiences has not identified differences in responses between the elderly and younger patients. In general, dose selections for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of concomitant disease or other drug therapy including beta blockers.²

HOW SUPPLIED

Mite extracts in 50% Glycero-Coca solution are supplied as follows:

- D. farinae: 5,000 Allergy Unit/mL, 10, 30, and 50 mL vials NDC 22840-0033
- D. farinae: 10,000 Allergy Unit/mL, 10, 30, and 50 mL vials NDC 22840-0034
- D. farinae: 30,000 Allergy Unit/mL, 10, 30, and 50 mL vials NDC 22840-0038
- D. pteronyssinus 5,000 Allergy Unit/mL, 10, 30, and 50 mL vials NDC 22840-0035
- D. pteronyssinus: 10,000 Allergy Unit/mL, 10, 30, and 50 mL vials NDC 22840-0036
- D. pteronyssinus: 30,000 Allergy Unit/mL, 10, 30, and 50 mL vials NDC 22840-0039
- D. farinae/D. pteronyssinus 5,000 Allergy Unit/mL each species, 10, 30, mixture: and 50 mL vials NDC 22840-0037
- D. farinae/D. pteronyssinus 15,000 Allergy Unit/mL each species, 10, 30, mixture: and 50 mL vials NDC 22840-0040
- D. farinae: 10,000 Allergy Unit/mL, 5 mL percutaneous NDC 22840-0034 test vial D. pteronyssinus: 10,000 Allergy Unit/mL, 5 mL percutaneous NDC 22840-0036 test vial
- D. farinae/D. pteronyssinus 5,000 Allergy Unit/mL each species, 5 mL mixture: percutaneous test vial NDC 22840-0037

STORAGE AND HANDLING SECTION

Store dust mite extract at 2°-8°C (36° to 46°F).

Keep dust mite extract at 2°- 8°C (36° to 46°F) during office use.

Dilutions of concentrated extract result in a glycerin content of less than 50% which results in reduced stability of the extracts. 1:100 dilutions should be kept no longer than a month, and more dilute solutions no more than a week. The potency of a dilution can be checked by skin test comparison to a fresh dilution of the extract on a known mite allergic individual.

REFERENCES

1. Bernstein IL, Li JT, Bernstein DI, et al. Allergy diagnostic testing: an updated practice parameter. *Ann Allergy Asthma Immunol* 2008; 100:S1148.
2. Cox L, Li JT, Nelson H, Lockey R. Allergen immunotherapy: A practice parameter second update. *J Allergy Clin Immunol* 2007; 120:S25-S85.
3. Amin HS, Liss GM, Bernstein DI. Evaluation of near-fatal reactions to allergen immunotherapy injections. *J Allergy Clin Immunol* 2006; 117: 169-75.
4. Lockey RF, Benedict LM, Turkeltaub PC, Bukantz SC. Fatalities from immunotherapy (IT) and skin testing (ST). *J Allergy Clin Immunol* 1987; 79:660-77.
5. Reid MJ, Lockey RF, Turkeltaub PC, Platts-Mills TA. Survey of fatalities from skin testing and immunotherapy 1985-1989. *J Allergy Clin Immunol* 1993;92:6-15.
6. Bernstein DI, Wanner M, Borish L, Liss GM. Twelve-year survey of fatal reactions to allergen injections and skin testing: 1990-2001. *J Allergy Clin Immunol* 2004; 113:1129-36.
7. Lockey RF, Nicoara-Kasti GL, Theodoropoulos DS, Bukantz SC. Systemic reactions and fatalities associated with allergen immunotherapy. *Ann Allergy Asthma Immunol* 2001;87(suppl 1): 47-55.
8. Malling HJ. Minimising the risks of allergen-specific injection immunotherapy. *Drug Saf* 2000;23:323-332.
9. Greenberg MA, Kaufman CR, Gonzalez GE, et. al. Late and immediate systemic-allergic reactions to inhalant allergen immunotherapy. *J Allergy Clin Immunol* 1986;77:865-870.
10. Jacobs RL, Rake GW, Jr., Fournier DC, Chilton RJ, Culver WG, Beckmann CH. Potentiated anaphylaxis in patients with drug-induced beta-adrenergic blockade. *J Allergy Clin Immunol* 1981;68:125-7.
11. Arlian L, Bernstein D, Bernstein L, et al. Prevalence of dust mites in the homes of people with asthma living in eight different geographic areas of the United States. *J Allergy Clin Immunol* 1992;90:292-300.
12. Chapman MD, Platts-Mills TA, Gabriel M, et al. Antibody response following prolonged hyposensitization with *Dermatophagoides pteronyssinus* extract. In *Arch Allergy Appl Immunol* 1980;61:431-40.
13. Gurka G, Rocklin R. Immunologic responses during allergen-specific immunotherapy for respiratory allergy. *Ann Allergy* 1988;61:239-45.
14. Voorhorst R, Spijksma FTM, Varekamp H. House Dust Atopy and the House Dust Mite. Leiden: Stafleu's Scientific Publishing Co; 1969.
15. Maunsell K, Wraith DG, Hughes AM. Hyposensitisation in mite asthma. *Lancet* 1971;1:967-8.
16. Mite Allergy Subcommittee of the Research Committee of the British Thoracic Association. A trial of house dust mite extract in bronchial asthma. *Br J Dis Chest* 1979;73:260-70.
17. Abramson MJ, Puy RM, Weiner JM. Is allergen immunotherapy effective in asthma? A meta-analysis

of randomized controlled trials. Am J

Respir Crit Car Med 1995;151:969-74.

18. Abramson M, Puy R, Weiner J. Immunotherapy in asthma: an updated systematic review. Allergy 1999;54:1022-41.

19. Abramson MJ, Puy RM, Weiner JM. Allergen immunotherapy for asthma. The Cochrane Database of Systematic Reviews 2003;CD001186.

20. Bousquet J, Calvayrac P, Guerin B, et al. Immunotherapy with a standardized Dermatophagoides pteronyssinus extract. I. In vivo and in vitro parameters after a short course of treatment. J Allergy Clin Immunol 1985;76:734-44.

21. Garcia-Ortega P, Merelo A, Marrugat J, Richart C. Decrease of skin and bronchial sensitization following short-intensive scheduled immunotherapy in mite-allergic asthma. Chest 1993;103:183-7.

THIS KIT CONTAINS:

5 x 5mL empty colored vials

1 x 30mL normal saline

1 x 5mL Std. Dermatophagoides Pteronyssinus Allergen Extract

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

Rx ONLY

Packaged By:

Alvix Laboratories, LLC

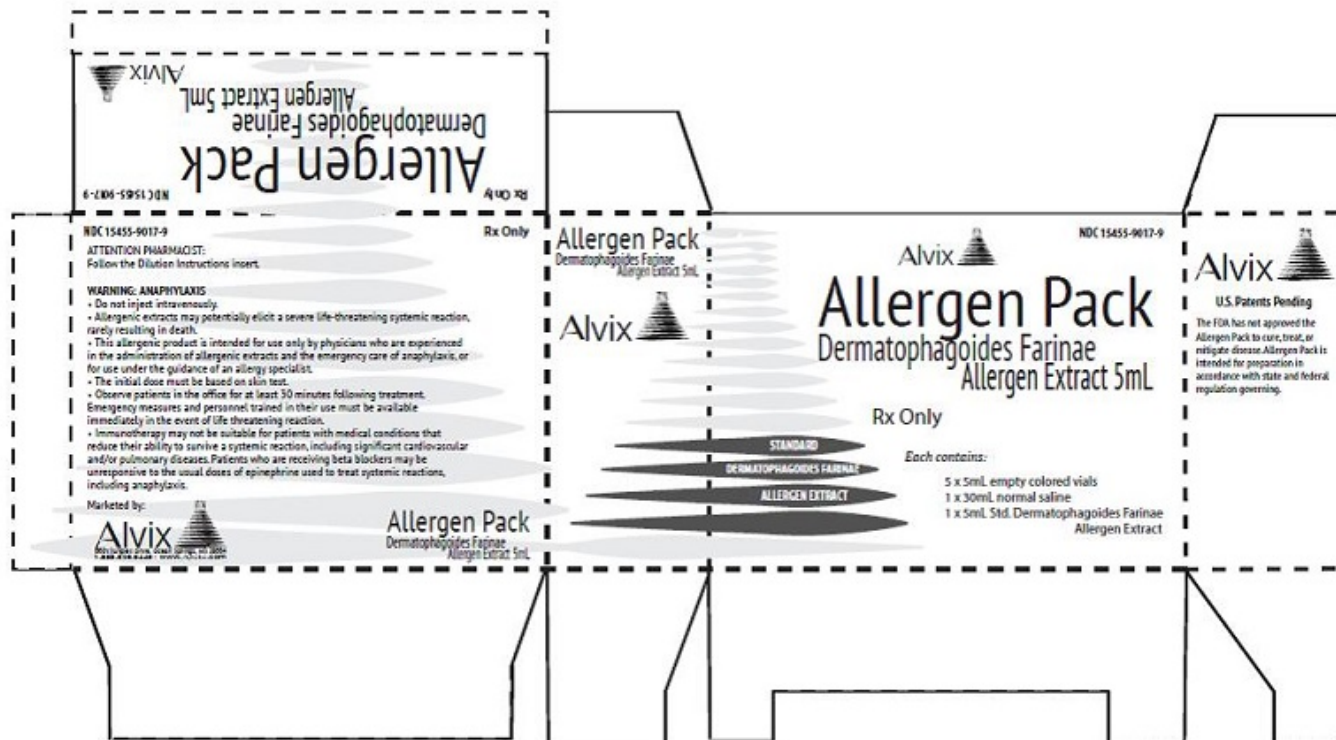
6601 Sunplex Dr.

Ocean Springs, MS 39564

1.888.526.5449

www.Alvix.com





ALLERGEN PACK DERMATOPHAGOIDES FARINAE

allergen pack dermatophagoides farinae kit

Product Information

Product Type	STANDARDIZED ALLERGENIC	Item Code (Source)	NDC:15455-9017
--------------	-------------------------	--------------------	----------------

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:15455-9017-9	1 in 1 CARTON; Type 1: Convenience Kit of Co-Package		

Quantity of Parts

Part #	Package Quantity	Total Product Quantity
Part 1	1	
Part 2	1	

Part 1 of 2

NORMAL SALINE

normal saline solution

Product Information

Route of Administration	INTRADERMAL, SUBCUTANEOUS	DEA Schedule
-------------------------	---------------------------	--------------

Active Ingredient/Active Moiety		
Ingredient Name	Basis of Strength	Strength
SODIUM CHLORIDE (UNII: 451W47IQ8X) (CHLORIDE ION - UNII:Q32ZN48698)	SODIUM CHLORIDE	0.9 g in 1 mL

Inactive Ingredients	
Ingredient Name	Strength
WATER (UNII: 059QF0KO0R)	

Marketing Information			
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
unapproved drug other			

Part 2 of 2
ALLERGEN PACK DERMATOPHAGOIDES FARINAE
allergen pack dermatophagoides farinae extract

Product Information			
Route of Administration	SUBCUTANEOUS, INTRADERMAL	DEA Schedule	

Active Ingredient/Active Moiety		
Ingredient Name	Basis of Strength	Strength
DERMATOPHAGOIDES FARINAE (UNII: PR9U2YPF3Q) (DERMATOPHAGOIDES FARINAE - UNII:PR9U2YPF3Q)	DERMATOPHAGOIDES FARINAE	15000 [AU] in 1 mL

Inactive Ingredients	
Ingredient Name	Strength
GLYCERIN (UNII: PDC6A3C0OX)	
PHENOL (UNII: 339NCG44TV)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
SODIUM BICARBONATE (UNII: 8MDF5V39QO)	
WATER (UNII: 059QF0KO0R)	

Marketing Information			
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101834	07/21/2015	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101834	07/21/2015	

Labeler - Alvix Laboratories, LLC (962445925)

Registrant - Alvix Laboratories, LLC (962445925)

Revised: 7/2015

Alvix Laboratories, LLC